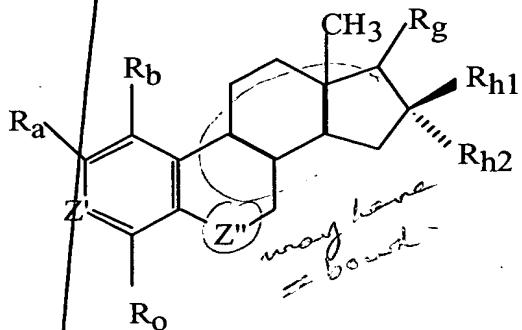


CLAIMS

We claim:

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A compound of the general formula:



wherein:

a) R_b and R_o are independently $-H$, unless otherwise noted to be $-Cl$, $-Br$, $-I$, $-F$, $-CN$, lower alkyl, $-OH$, $-OR_6$, $-CH_2-OH$, $-NH_2$, or $N(R_6)(R_7)$, wherein R_6 and R_7 are independently hydrogen or an alkyl or branched alkyl with up to 10 carbons; NO_2 ?

15 b) R_a is $-N_3$, $-C\equiv N$, $-CH_2-C\equiv R$, $-C\equiv C-R$, $-C=CH-R$, $-R-C=CH_2$, $-C\equiv CH$, $-CH_2-C\equiv N$, $>C(H)-C(O)-OR_3$, $-O-R$, $-R-R_1$, $-O-R-R_1$, $OR(O)R$, $OR(O)R_1$, ROR , ROR_1 , $-NHC(O)R_6$, $-NRC(O)R_6$, $-NH_2$, or $N(R_6)(R_7)$, wherein R_6 and R_7 are independently hydrogen or an alkyl or branched alkyl with up to 10 carbons; or a hetero group wherein the hetero group may have more than one hetero atom and may be substituted, where R is H or a straight or branched alkyl with up to 10 carbons or aralkyl, and in any position F may be substituted in or on the carbon chain, and R_1 is $-OH$, $-NH_2$, $-Cl$, $-Br$, $-I$, $-F$ or CF_3 when R_1 is terminal;

20 c) Z' is $>COH$, unless otherwise noted to be $>C-OAc$;

d) $>C-R_g$ is $>CH_2$, $>C(H)-OH$, $>C=O$, $>C=N-OH$, $>C(R_3)OH$, $>C=N-OR_3$, $>C(H)-NH_2$, $>C(H)-NHR_3$, $>C(H)-NR_3R_4$, or $>C(H)-C(O)-R_3$, where each R_3 and R_4 is independently an alkyl or branched alkyl with up to 10 carbons or aralkyl; or

25 R_g is i) an alkyl of 1-10 carbon atoms that is straight chain or branched, ii) an alkenyl of 1-10 carbon atoms that is straight chain or branched having one or more double bonds at

any position from C to Z₀, iii) an alkenyl group of 1-10 carbon atoms that is straight chain or branched having one or more triple bonds at any position where chemically possible, iv) a mono or dialkyl amino group wherein each alkyl chain has from 1-10 carbon atoms and is straight chain or branched, v) (CH₂)_n-CF₂-, (CH₂)_n-CR₁ or (CH₂)_n-CF₃ wherein n=0-10 carbons, or vi) H, and wherein any of i-iv are optionally substituted with an aromatic or heteroaromatic group or optionally substituted with a heterogroup and wherein R_g is either in the α or β position and; or

R_g is R_{g1} and R_{g2}, and wherein R_{g1} may be present or absent and when present is -H, an alkyl, alkenyl, or alkynyl of 1-10 carbon atoms that is straight chain or branched and is 10 optionally substituted, and R_{g2} is a hetero group, wherein when R_{g1} is absent the heterogroup is bonded to the 17-position with a double bond, and wherein either R_{g1} or R_{g2} can be in the β position with the other group in the α position, and R₁ is -OH, -NH₂, -Cl, -Br, -I, -F or CF₃ when R₁ is terminal;

e) R_{h1} and R_{h2} are independently H, unless otherwise noted to be a straight or branched chain alkyl, alkenyl or alkynyl with up to 10 carbons that is unsubstituted, or substituted with one or more groups selected from a hetero functionality that is either not substituted, mono-substituted or multiply substituted with an alkyl, alkenyl or alkynyl chain up to 10 carbons; a halo functionality (F, Cl, Br or I); an aromatic group optionally substituted with at least one hetero, halo or alkyl; or R_{h1} and R_{h2} are independently a group containing at least one aliphatic or aromatic group optionally substituted with at least one hetero, halo or alkyl;

f) Z" is >CH₂;

and wherein saturated bonds in any ring may be dehydrogenated;

and wherein all monosubstituted substituents have either an α or β configuration;

and wherein lower alkyl is defined as a carbon chain having 1-10 carbon atoms which 25 may be branched or unbranched.

2. The compound of Claim 1, wherein :

R_a is -OCH₃; and

R_{g1} and R_{g2} are each H.

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3. The compound of Claim 1, wherein :

R_a is -OCH₃; and

R_g is =CH₂.

*Sub 4
5 B2*

The compound of Claim 1, wherein :

R_a is -OCH₃;

R_{g1} is absent; and

R_{g2} is =NOH.

5. The compound of Claim 1, wherein :

R_a is -OCH₂;

R_{g1} is β -H; and

10 R_{g2} is α -OH.

6. The compound of Claim 1, wherein :

R_a is -OCH₃;

R_{g1} is -H; and

R_{g2} is -NH₂.

7. The compound of Claim 1, wherein :

R_a is -OCH₃;

Z' is >C-OAc;

R_{g1} is -H; and

R_{g2} is -OAc.

8. The compound of Claim 1, wherein :

R_a is -OCH₃;

25 R_{g1} is -H; and

R_{g2} is -CH₂CH₂CH₃.

9. The compound of Claim 1, wherein :

R_a is -OCH₃;

30 R_{g1} is -H; and

R_{g2} is -CH₃.

10. The compound of Claim 1, wherein :

R_a is -OCH₃; and

R_g is =CHCH₂CH₃.

5 11. The compound of Claim 1, wherein :

R_a is -OCH₃;

R_{g1} is -H; and

R_{g2} is -NHCH₂CH₂CH₃.

10 12. The compound of Claim 1, wherein :

R_a is -OCH₃; and

R_g is =CHCH₃.

13. The compound of Claim 1, wherein :

R_a is -OCH₃;

R_{g1} is -H; and

R_{g2} is -CH₂CH₃.

14. The compound of Claim 1, wherein :

R_a is -OCH₃; and

R_g is =N-NH-(SO₂)-C₆H₄-p-CH₃.

15. The compound of Claim 1, wherein :

R_a is -OCH₃;

R_{g1} is H; and

R_{g2} is -COOH.

Stefus?

16. A method of modifying estradiol analogs for preventing or hindering demethylation, oxidation and conjugation with another molecule during metabolism.

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17. The method claim 16 wherein the method comprises adding steric bulk or modification of chemical or electrostatic characteristics or a combination thereof to estradiol analogs for retarding or preventing metabolic deactivation.

18. The compound of Claim 1, wherein:

R_a is -OCH₃;

>C-R_{g1} is >CH;

>C-R_{g2} is >COH; and

R_{h1} and R_{h2} are independently -H and Et.

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19. The compound of Claim 1, wherein:

R_a is -OCH₃;

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>C-R_{g1} is >CH;

>C-R_{g2} is >COH; and

R_{h1} and R_{h2} are independently H and n-Pr.

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20. The compound of Claim 1, wherein:

R_a is -OCH₃;

>C-R_{g1} is >CH;

>C-R_{g2} is >COH; and

R_{h1} and R_{h2} are independently H and i-Bu.

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21. The compound of Claim 1, wherein:

R_a is -OCH₃;

>C-R_{g1} is >CH;

>C-R_{g2} is >COH; and

R_{h1} and R_{h2} are independently H and CH₂OH.

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22. The compound of Claim 1, wherein :

R_a is -OCH₃;

>C-R_{g1} is >CH;

>C-R_{g2} is >COH; and

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R_{h1} and R_{h2} are independently H and n-Bu.

23. The compound of Claim 1, wherein :

R_a is -OCH₃;
>C-R_{g1} is >CH;
>C-R_{g2} is >COH; and

5 Z" is >CH₂, and

R_{h1} and R_{h2} are independently H and Me.

24. The compound of Claim 1, wherein :

R_a is -OCH₃;
>C-R_{g1} is >CH;
>C-R_{g2} is >COH; and

10 R_{h1} and R_{h2} are independently H and -CH₂N(CH₃)₂.

25. The compound of Claim 1, wherein :

R_a is -C(O)CH₃;
>C-R_{g1} is >CH; and
>C-R_{g2} is >COH.

26. The compound of Claim 1, wherein :

R_a is -C(O)H;
>C-R_{g1} is >CH; and
>C-R_{g2} is >COH.

27. The compound of Claim 1, wherein :

25 R_a is -CH₂OH;
>C-R_{g1} is >CH; and
>C-R_{g2} is >COH.

28. The compound of Claim 1, wherein :

30 R_a is -NO₂;
>C-R_{g1} is >CH; and
>C-R_{g2} is >COH.

29. The compound of Claim 1, wherein :

R_a is $-N(CH_3)_2$;

>C-R_{g1} is >CH; and

>C-R_{g2} is >COH.

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30. The compound of Claim 1, wherein :

R_a is $-NH_2$;

>C-R_{g1} is >CH; and

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>C-R_{g2} is >COH.

31. The compound of Claim 1, wherein :

R_a is $-C\equiv C-CH_3$;

>C-R_{g1} is >CH; and

>C-R_{g2} is >COH.

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32. The compound of Claim 1, wherein :

R_a is $-CH_2CH_3$;

>C-R_{g1} is >CH; and

>C-R_{g2} is >COH.

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33. The compound of Claim 1, wherein :

R_a is $-CH_3$;

>C-R_{g1} is >CH; and

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>C-R_{g2} is >COH.

34. The compound of Claim 1, wherein :

R_a is $-NH_2$; and

R_{g1} and R_{g2} are each H.

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35. The compound of Claim 1, wherein :

R_a is $-C(O)NH_2$; and

R_{g1} and R_{g2} are each H.

5 36. The compound of Claim 1, wherein :
Ra is $-\text{NH}_2^+\text{CH}_3$; and
Rg1 and Rg2 are each H.

37. The compound of Claim 1, wherein :
 R_a is $-N(CH_3)_2$; and
 R_{g1} and R_{g2} are each H.

38. The compound of Claim 1, wherein :
R_a is -NH⁺(CH₃)₂ (or N(CH₃)₂•HCl); and
R_{g1} and R_{g2} are each H.

39. The compound of Claim 1, wherein :

R_a is $-NH^+(CH_3)_2$ or $N(CH_3)_2-HCl$; and

$>C-R_g1$ is $>CH$; and

$>C-R_g2$ is $>COH$.

40. The compound of Claim 1, wherein :

R_a is -OCH₃;

>C-R_{g1} is >CH;

>C-R_{g2} is >COH; and

an olefin at C⁹ C¹¹

The compound of Claim 1, wherein :

R_a is $-OCH_2CH_3$;

R_g1 is absent; and

R_g2 is $=CHCH_3$.

48. The compound of Claim 1, wherein:
R_a is $-\text{CH}=\text{CHCH}_3$;
R_{g1} is absent; and
R_{g2} = CHCH_3 .

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49. The compound of Claim 1, wherein :

R_a is $-OCH_2CH_3$;

R_g1 is absent; and

$R_g2 = CH_2$.

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50. The compound of Claim 1, wherein :

R_a is $-C\equiv CCH_3$;

R_g1 is absent; and

$R_g2 = CH_2$.

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51. The compound of Claim 1, wherein :

R_a is $-C(O)H$;

R_g1 is absent; and

$R_g2 = CH_2$.

52. The compound of Claim 1, wherein :

R_a is $-NHC(O)H$;

R_g1 is absent; and

$R_g2 = CH_2$.

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53. The compound of Claim 1, wherein :

R_a is $-CH_2OH$;

R_g1 is absent; and

$R_g2 = CH_2$.

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54. The compound of Claim 1, wherein :

R_a is -CH₂CH₃;

R_{g1} is absent; and

R_{g2} =CH₂.

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55. The compound of Claim 1, wherein :

R_a is -CH₃;

R_{g1} is absent; and

R_{g2} =CH₂.

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56. The compound of Claim 1, wherein :

R_a is -CH=CHCH₃;

R_{g1} is absent; and

R_{g2} =CH₂.

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57. The compound of Claim 1, wherein :

R_a is -OCH₂CH₃; and

R_{g1} and R_{g2} are each H.

58. The compound of Claim 1, wherein :

R_a is -C≡CCH₃; and

R_{g1} and R_{g2} are each H.

59. The compound of Claim 1, wherein :

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R_a is -C(O)H; and

R_{g1} and R_{g2} are each H.

60. The compound of Claim 1, wherein :

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R_a is -NHC(O)H; and

R_{g1} and R_{g2} are each H.

61. The compound of Claim 1, wherein :

R_a is -CH₂OH; and

R_{g1} and R_{g2} are each H.

5 62. The compound of Claim 1, wherein :

R_a is -CH₂CH₃; and

R_{g1} and R_{g2} are each H.

63. The compound of Claim 1, wherein :

10 R_a is -CH₃; and

R_{g1} and R_{g2} are each H.

64. The compound of Claim 1, wherein :

R_a is -CH=CHCH₃; and

R_{g1} and R_{g2} are each H.

65. The compound of Claim 1, wherein :

R_a is -OCH₂CH₃;

R_{g1} is H; and

R_{g2} is CH₃.

66. The compound of Claim 1, wherein :

R_a is -C≡CCH₃;

R_{g1} is H; and

25 R_{g2} is CH₃.

67. The compound of Claim 1, wherein :

R_a is -C(O)H;

R_{g1} is H; and

30 R_{g2} is CH₃.

68. The compound of Claim 1, wherein :

R_a is -NHC(O);

R_{g1} is H; and

R_{g2} is CH₃.

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69. The compound of Claim 1, wherein :

R_a is -CH₂OH;

R_{g1} is H; and

R_{g2} is CH₃.

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70. The compound of Claim 1, wherein :

R_a is -CH₂CH₃;

R_{g1} is H; and

R_{g2} is CH₃.

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71. The compound of Claim 1, wherein :

R_a is -CH₃;

R_{g1} is H; and

R_{g2} is CH₃.

72. The compound of Claim 1, wherein :

R_a is -CH=CHCH₃;

R_{g1} is H; and

R_{g2} is CH₃.

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73. The compound of Claim 1, wherein :

R_a is -OCH₂CH₃;

R_{g1} is H; and

R_{g2} is CH₂CH₃.

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80. The compound of Claim 1, wherein :

R_a is $-\text{CH}=\text{CHCH}_3$;

R_{g1} is H; and

R_{g2} is CH_2CH_3 .

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86. The compound of Claim 1, wherein :

R_a is $-\text{CH}_2\text{CH}_3$;
 R_g1 is absent; and
 R_g2 is $=\text{CHCH}_2\text{CH}_3$.

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87. The compound of Claim 1, wherein :

R_a is $-\text{CH}_3$;
 R_g1 is absent; and
 R_g2 is $=\text{CHCH}_2\text{CH}_3$.

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88. The compound of Claim 1, wherein :

R_a is $-\text{CH}=\text{CHCH}_3$;
 R_g1 is absent; and
 R_g2 is $=\text{CHCH}_2\text{CH}_3$.

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89. The compound of Claim 1, wherein :

R_a is $-\text{OCH}_3$;
 R_g1 is H; and
 R_g2 is $-\text{CH}_2\text{OH}$.

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90. The compound of Claim 1, wherein :

R_a is $-\text{OCH}_3$;
 $>\text{C}-\text{R}_g1$ is $>\text{CH}$;
 $>\text{C}-\text{R}_g2$ is $>\text{COH}$; and
an olefin at C6-C7.

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91. The compound of Claim 1, wherein :

R_a is $-\text{N}_3$; and
 $>\text{C}-\text{R}_g$ is $>\text{CH}$.

92. The compound of Claim 1, wherein :

R_a is H; and
 $>\text{C}-\text{R}_g$ is $>\text{CH}$.

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